Based on an intention-to-treat analysis, the study found no difference in G4PFS between PemC and PCB (median 3.9 vs 2.9 months; HR, 0.85; 90% CI, 0.70 to 1.04; log-rank p=0.176).

In addition, the study found no differences between PemC and PCB in PFS (median 4.4 vs 5.5 months; HR, 1.06; 95% CI, 0.84 to 1.35; log-rank p=0.610), OS (median 10.5 vs 11.7 months; HR, 1.07; 95% CI, 0.83 to 1.36; log-rank p=0.616), RR (23.6% vs 27.4%; p=0.414), or DCR (59.9% vs 57.0%; p=0.575).

Based on the actual study regimen of 171 patients treated with PemC and 166 treated with PCB, the study found that the PemC group had significantly more drug-related Grade 3/4 anemia (18.7% vs 5.4%; p<0.001) and thrombocytopenia (24.0% vs 9.6%; p<0.001). Patients treated with PCB had significantly more drug-related Grade 3/4 neutropenia than the PemC group (48.8% vs 24.6%; p<0.001) and Grade 1 and Grade 2 alopecia (16.3% vs 5.8%;p=0.003; and 12.0% vs 2.3%; p<0.001, respectively).

According to the investigators, there were no unexpected toxicities and both treatments demonstrated tolerability.

RIGHT Study Results

Written by **Maria Vinall**

Rechallenge of imatinib significantly improves progression-free survival (PFS) and disease control rate (DCR) in patients with advanced gastrointestinal stromal tumor (GIST) after the failure of at least imatinib and sunitinib, likely by continuous kinase inhibition of the bulk of disease clones which retain imatinib sensitivity. Tyrosine-kinase inhibitor (TKI)-resistant clones continue to progress, however, resulting in a relatively brief duration of benefit.

Despite having received highly effective treatments such as imatinib and sunitinib, >80% of patients with advanced GIST experience disease progression. Based on evidence of rapid GIST progression after discontinuation of all TKIs, common practice has been to resume imatinib therapy in these patients, even though the efficacy of this approach has not been proven in prospective clinical trials. Yoon-Koo Kang, MD, PhD, University of Ulsan College of Medicine, Seoul, South Korea, presented data from the Rechallenge of Imatinib in GIST Having No Effective Treatment study [RIGHT; NCT01151852; Kang YK et al. *J Clin Oncol* 2013 (suppl; abstr LBA10502)], which evaluated the efficacy of imatinib rechallenge in patients with advanced GIST following failure of all TKIs.

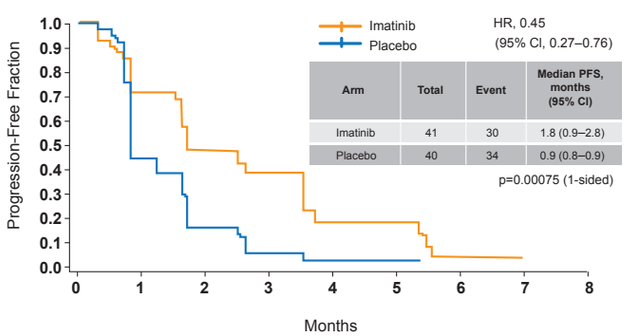
Eligible patients included adults with metastatic and/or unresectable GIST and prior benefit from first-line imatinib (defined as complete response [CR], partial response [PR], or stable disease [SD] for >6 months on imatinib 400 mg/day) and disease progression with at least both first-line imatinib and second-line sunitinib. Stratification was based on ECOG PS (0 to 1 vs 2 to 3) and use of third-line TKI. Subjects were randomized to receive oral imatinib 400 mg QD or placebo.

At the time of disease progression, subjects in the placebo group were permitted to cross over to open-label imatinib. Subjects receiving imatinib were permitted to continue or stop imatinib. The primary study endpoint was PFS determined by blinded external radiology review according to RECIST v1.0. Response was evaluated by computed tomography, every 4 weeks for the first 4 months then every 8 weeks until disease progression or death. Secondary endpoints included disease control rate (DCR: CR+PR+SD) at 12 weeks, overall survival (OS), time to progression, and safety.

Between July 2010 and January 2013, 81 patients were randomized (imatinib, n=41; placebo, n=40) at a single Korean center. More than 65% of the study participants were men; the median age was 60 years. Approximately 40% of subjects had received ≥3 prior TKIs. The small bowel was the most common disease site followed by the stomach. About 60% of patients had received imatinib as first-line therapy for >2 years.

At study end in March 2013, median PFS was significantly longer for patients randomized to imatinib (1.8 months) versus placebo (0.9 months; HR, 0.45; 95% CI, 0.27 to 0.76; p=0.00075; Figure 1). The HR was <0.6 for all of the preplanned subgroups, strongly favoring imatinib. DCR at 12 weeks was 31.7% for imatinib versus 5% for placebo (p=0.003). The median PFS for the 37 subjects in the placebo arm who crossed over to imatinib after progression was 1.7 months, indicating the limited duration of the treatment response. Median OS was 8.2 months for imatinib versus 7.5 months for placebo (HR, 0.99; p=0.4912; Figure 2). The most common Grade 3 or higher treatment-emergent AEs during the double-blind period in the imatinib arm included anemia (29%), fatigue (10%), and hyperbilirubinemia (7%).

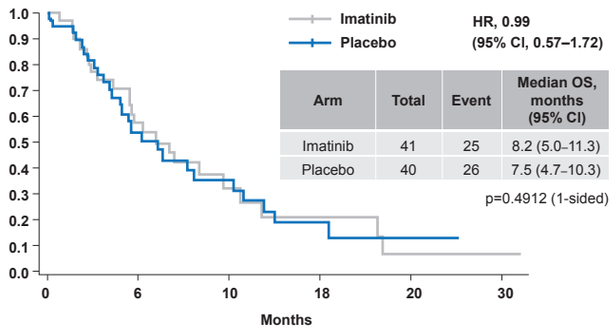
Figure 1. Progression-Free Survival



PFS=progression-free survival.

Reproduced with permission from YK Kang, MD, PhD.

Figure 2. Overall Survival



Reproduced with permission from YK Kang, MD, PhD.

Results From the EURAMOS-1 Trial

Written by Maria Vinall

Results from the Combination Therapy, PEG-Interferon Alfa-2b, and Surgery in Treating Patients With Osteosarcoma trial [EURAMOS-1; NCT00134030; *J Clin Oncol* 2013 (suppl; abstr LBA10504)] show that maintenance therapy with pegylated interferon α-2b (PEG IFN-α-2b) after surgery and chemotherapy does not improve event-free survival (EFS) in patients with high-grade osteosarcoma and good response to preoperative methotrexate, doxorubicin, and cisplatin (regimen collectively called MAP).

EURAMOS-1 is a randomized controlled trial from the European and American Osteosarcoma Study Group that investigated the efficacy of maintenance therapy with PEG IFN-α-2b in patients with resectable osteosarcoma and "good response" (<10% viable tumor at surgery) to preoperative chemotherapy. The results were presented by Stefan S. Bielack, MD, PhD, Klinikum Stuttgart Olgahospital, Stuttgart, Germany.

Osteosarcoma is a rare cancer, with 2 to 3 cases per million per year, in which histologic response is a prognostic factor for survival. Poor responders are generally considered to have a 3-year EFS and 5-year overall survival (OS) rate of 45% each [Ritter J, Bielack SS. *Ann Oncol* 2010]. Among good responders, those rates climb to 70%. IFN-α has shown growth inhibition in osteosarcoma cell lines, animal studies have extensively studied it in other tumors as maintenance therapy, and its safety in children is well established. These factors combined with the relatively favorable prognosis for patients with good histologic response may make IFN-α a reasonable option for maintenance therapy.

Patients aged ≤40 years who had resectable localized or primary metastatic high-grade extremity or axial osteosarcoma were eligible for registration at diagnosis, provided they had no pretreatment for osteosarcoma and no prior chemotherapy. All patients received 2 cycles of MAP induction followed by surgical resection. Good histologic responders were then randomized to 4 cycles of MAP alone (MAP group) or 4 cycles of MAP followed by PEG IFN-α-2b weekly from Week 30 to Week 104 (MAP-IFN group). The starting dose of PEG IFN-α-2b was 0.5 μg/kg/week (maximum of 50 μg) given subcutaneously for 4 weeks. If the drug was well tolerated, the dose could be escalated to 1.0 μg/kg/week (maximum of 100 μg). The primary study endpoint was EFS, defined as death, local recurrence, new metastatic disease, progression, or secondary malignancy. Secondary endpoints were OS, toxicity, and quality of life.

A total of 2260 patients were registered between April 2005 and November 2011, which makes it the largest trial studying this rare cancer. Good response was confirmed in 1041 patients, of which 715 (male, 59%; median age, 14 years) consented to randomization (MAP, n=358; MAP-IFN, n=357). Of the 357 patients randomized to the MAP-IFN group, 271 (76%) started treatment with PEG IFN-α-2b at a median of 5.4 months after randomization. The primary reason for not starting PEG IFN-α-2b was refusal (66/86 patients).

Grade 0 to 2 toxicities were reported by 70% (n=187) of patients receiving PEG IFN-α-2b while 30% (n=81) reported Grade 3 or 4 toxicities. Grade 4 toxicities included 13 hematologic, 3 cardiac, and 1 each dyspnea, mood alteration, and amylase. At study end, 37 were still receiving PEG IFN-α-2b while 234 subjects had stopped it (128 had completed therapy; 106 terminated early). Reasons for early termination were toxicity (n=44), disease progression (n=25), and refusal/other (n=37). The median duration of PEG IFN-α-2b therapy was 14.9 months. After a median follow-up of 3 years following randomization, there was no significant difference in EFS between the MAP and MAP-IFN groups (74% vs 77%; HR, 0.82; 95% CI, 0.61 to 1.11; p=0.201).

In conclusion, MAP plus maintenance therapy with PEG IFN-α-2b was not superior to MAP alone, but it should be noted that the results may have been influenced by the failure of 24% of patients to start PEG IFN-α-2b treatment. Further follow-up for events and survival is ongoing.